## REMARKS

Claims 29-55 are currently pending and presented for examination. Applicants respectfully request that the Examiner reconsider the rejection of claims 29-55 in view of the remarks set forth below.

Rejection of claims 29, 30, 33, 34, 38-45 and 48-52 under 35 U.S.C. § 102(e)

The Examiner rejects claims 29, 30, 33, 34, 38-45 and 48-52 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,340,588 (Nova et al.). In particular, the Examiner asserts that Nova et al. disclose a method of detecting the presence or absence of a plurality of different target analytes as recited in independent claim 29, including the step of dipping the projections of the second substrate into said assay wells of the first substrate, wherein the projections of the second substrate each comprise a plurality of discrete sites that comprise different bioactive agents, and wherein the assay wells of the first substrate comprise a plurality of different target analytes. The Examiner also asserts that Nova et al. disclose each of the additional elements recited in claims 30, 33, 34, 38-45 and 48-52, each of which depend from independent claim 29.

Applicants maintain that Nova et al. do not disclose all of the elements of any of claims 29, 30, 33, 34, 38-45 or 48-52, and thus, do not anticipate any of these claims under 35 U.S.C. § 102(e). As discussed during the interview of September 4, 2008, Nova et al. disclose compositions and methods for tagging a molecule attached to a matrix with a memory. In the methods disclosed by Nova et al., each of the tagged molecules can be distinguished from each other by virtue of the memory tag specific for the molecule. This tagging further permits a single molecule to be tracked to a particular matrix, or position on a matrix, during manipulations by virtue of its corresponding memory tag, which is specific for that molecule. Although Nova et al. disclose various shapes and materials that can be used for matrices, Nova et al. do not disclose dipping the projections of a second substrate into the assay wells of a first substrate, wherein the assay wells of the first substrate each comprise a plurality of different target analytes, and wherein the second substrate comprises a plurality of array locations, each array location comprising a plurality of discrete sites on a projection, wherein the sites comprise different bioactive agents. Applicants have thoroughly read Nova et al. in its entirety have found seven

locations where the act of dipping is described. As discussed in detail below, none of these sections disclose the step of dipping as set forth in independent claim 29.

The first occurrence of dipping, which appears at column 10, lines 31-49, states the following:

> Since matrix materials have many known uses in conjunction with molecules and biological particles, there are a multitude of methods known to artisans of skill in this art for linking, joining or physically contacting the molecule or biological particle with the matrix material. In some embodiments, the recording device with data storage unit is placed in a solution or suspension of the molecule or biological particle of interest. In some of such instances, the container, such as the microtiter plate or test tube or other vial, is the matrix material. The recording device is placed in or on the matrix or is embedded, encased or dipped in the matrix material or otherwise place in proximity by enclosing the device and matrix material in a sealed pouch or bag or container [MICROKAN™] fabricated from, preferably, porous material, such as polytetrafluoroethylene [marketed under the trademark TEFLON® (Trademark, E. I. DuPont)] or polypropylene prepared with pores, that is inert to the reaction of interest and that have pores of size permeable to desired components of the reaction medium.

Column 10, lines 31-49.

The above section of the Nova et al. reference discloses methods for making a matrix comprising both a biological molecule and a memory by dipping a recording device with data storage (the memory) into a matrix material that contains the biological molecule. This method permits the memory to be associated with, and thus capable of identifying, the particular type of biological molecule that is present at a particular location on the matrix. This disclosure of dipping does not teach that the matrix includes locations that each comprise a plurality of different target analytes or that the a memory that is dipped into a matrix location is a projection

of a second substrate, wherein the projection comprises an array location comprising a plurality of discrete sites, wherein the sites comprise different bioactive agents. Rather, this disclosure of dipping describes a method for associating a programmable memory device with a matrix material containing a biological molecule..

The second occurrence of dipping, which appears at column 14, lines 19-42, states the following:

> In particular, methods for tagging constituent members of combinatorial libraries and other libraries or mixtures of diverse molecules and biological particles are provided. These methods involve electromagnetically tagging or optically imprinting molecules, particularly constituent members of a library, by contacting the molecules or biological particles or bringing such molecules or particles into proximity with a matrix with memory and programming the memory [by writing to it or by imprinting the matrix with an optical bar code or by associating a pre-engraved code with identifying information with retrievable information from which the identity, synthesis history, batch number or other identifying information can be retrieved. The contact is preferably effected by coating, completely or in part, the recording device with memory with the matrix and then linking, directly or via linkers, the molecule or biological particle of interest to the matrix support. The memories can be coated with a protective coating, such as a glass or silicon, which can be readily derivatized for chemical linkage or coupling to the matrix material. In other embodiments, the memories can be coated with matrix, such as for example dipping the memory into the polymer prior to polymerization, and allowing the polymer to polymerize on the surface of the memory.

Column 14, lines 19-42.

The above section of the Nova et al. reference discloses an alternative method for making a matrix comprising a memory and molecule or biological particle. In particular, the method describes coating a memory with a matrix by dipping the memory into a matrix material that is allowed to polymerize on the surface of the memory. The molecule or biological particle of interest is then linked to the matrix with memory. This disclosure of dipping does not teach that the memory is a projection of a second substrate, wherein the projection comprises an array location comprising a plurality of discrete sites, wherein the sites comprise different bioactive agents or that the material into which the memory is dipped comprises a plurality of different target analytes. Rather, this disclosure simply describes a particular method for associating a memory with a matrix by the dipping a programmable memory device into a matrix material, which is then allowed to polymerize over the memory, thereby permitting association of the matrix with the memory.

The third occurrence of dipping, which appears at column 37, lines 17-29, states the following:

> The data storage device with programmable memory may be coated with a material, such as a glass or a plastic, that can be further derivatized and used as the support or it may be encased, partially or completely, in the matrix material, such as during or prior to polymerization of the material. Such coating may be performed manually or may be automated. The coating can be effected manually or using instruments designed for coating such devices. Instruments for this purpose are available Isee, e.g., the Series C3000 systems for dipping available from Specialty Coating Systems, Inc., Indianapolis, Ind.; and the Series CM 2000 systems for spray coating available from Integrated Technologies, Inc. Acushnet, Mass.].

Column 37, lines 17-29.

The above section of the Nova et al. reference is a further elaboration of the section at column 14, lines 19-42. As described in the section appearing at column 14, lines 19-42, this section discusses coating the memory with a matrix material. In particular, this section discusses devices made for use in dip coating processes and devices for use in spray coating processes. This disclosure, however, does not teach that the memory is a projection of a second substrate, wherein the projection comprises an array location comprising a plurality of discrete sites, wherein the sites comprise different bioactive agents or that the material into which the memory is dipped comprises a plurality of different target analytes. As with the disclosure at column 14, lines 19-42, this disclosure simply describes a particular method for associating a memory with a matrix by the dipping a programmable memory device into a matrix material so that it becomes coated with the matrix material.

The forth occurrence of dipping, which appears at column 38, lines 9-14, states the following:

> The data storage devices with memory may be coated either directly or following coating with a ceramic, glass or other material, may then be coated with agarose, which is heated, the devices are dipped into the agarose, and then cooled to about room temperature. The resulting glass, silica, agarose or other coated memory device, may be used as the matrix supports for chemical syntheses and reactions.

Column 38, lines 9-14.

The above section of the Nova et al. reference discloses coating a memory with agarose. In particular, the method describes coating an uncoated or pre-coated memory with agarose by dipping the memory into molten agarose. This disclosure of dipping does not teach that the memory is a projection of a second substrate, wherein the projection comprises an array location comprising a plurality of discrete sites, wherein the sites comprise different bioactive agents or that the material into which the memory is dipped comprises a plurality of different target analytes. Rather, this disclosure simply describes coating the memory with an agarose layer.

The fifth occurrence of dipping, which appears at column 39, line 57 to column 40, line 3, states the following:

> There are innumerable synthetic matrices and methods for their preparation known to those of skill in this art. Synthetic matrices are typically produced by polymerization of functional matrices, or copolymerization from two or more monomers of from a synthetic monomer and naturally occurring matrix monomer or polymer, such as agarose. Before such polymers solidify, they are contacted with the data storage device with memory, which can be cast into the material or dipped into the material. Alternatively, after preparation of particles or larger synthetic matrices, the recording device containing the data storage unit(s) can be manually inserted into the matrix material. Again, such devices can be pre-coated with glass, ceramic, silica or other suitable material.

Column 39, line 57 to column 40, line 3.

The above section of the Nova et al. reference discloses methods for preparing matrices. The matrices can be associated with memories during their preparation or subsequent to their preparation. This section particularly describes the production of matrices made by the polymerization of monomers. With respect to the association of memories, it states that a memory can be contacted with the matrix material before it solidifies by casting or dipping the memory into the material. As an alternative, it states that the memory can be manually inserted into the matrix material. Neither of these teachings, which describe how memory can be associated with the matrix material, disclose that the memory is a projection of a second substrate, wherein the projection comprises an array location comprising a plurality of discrete sites, wherein the sites comprise different bioactive agents or that the material into which the memory is dipped comprises a plurality of different target analytes. Rather, this disclosure further describes methods of associating a memory with a matrix.

The sixth occurrence of dipping, which appears at column 106, line 35 to column 107, line 2, states the following:

> A series of appropriately activated matrices with memories are arranged in an array, one or, preferably two dimensional. In one configuration, each chip is pre-programmed and placed in a specific location that is entered into its memory, such as an x-y coordinate. At least one surface of the memory with matrix is treated so that the transferred reagent binds. For example, a piece of nitrocellulose can be fixed to one side of the memory device. The resulting array is then contacted with a separation medium whereby each reagent of interest is transferred to and bound to the end of the matrix with memory such that the reagent location is known. The matrices are separated and pooled; multiple arrays may be pooled as long as source information is recorded in each memory. All matrices with memories are then contacted with detection agents that specifically bind to reagents in the mixture. The matrices with memories are passed through a reading device, either after an incubation for end point determinations or continuously for kinetic measurements. The reading devices is a device that can detect label, such as fluorescence, and an reader, such as an RF ready, that can query the memory and identify each matrix. The rate of binding and maximum binding and identify of bound reagents can be determined. Dot blots, for example, can be used in hybridoma analysis to identify clones that secrete antibodies of desired reactivity and to determine the relative affinities of antibodies secreted by different cell lines. Matrices with memories that are activated to bind immunoglobulins and with on-board information specifying their relative locations in the array are dipped in an array into the wells of microplates containing hybridoma cells. After incubation, they are withdrawn, rinsed, removed and exposed to labeled antigen. Matrices of desired specificity and affinity are selected and read thereby identifying the original wells containing the hybridoma cells that produce the selected antibodies.

Column 106, line 35 to column 107, line 2.

The above section of the Nova et al. reference discloses an array of matrices with memories that have a surface capable of binding a reagent. Each matrix with memory is then bound to a particular reagent, wherein the memory identifies the reagent that is bound. The matrices with memories can then be separated from the array and pooled in any combination or with matrices obtained from other arrays. The matrices with memories are then contacted with detection agents that bind to the reagents in the mixed pool of matrices The matrices are then run through a detector. A particular reagent that binds to a detector molecule can be identified by its association with a particular matrix since the memory identifies the reagent bound to that matrix. This general disclosure is further exemplified in connection with dot blots used for hybridoma analysis. Here, individual hybridoma cell lines are placed into separate wells of a microtiter plate. Each hybridoma cell line secretes a single type of monoclonal antibody. An array of matrices with memories, wherein each matrix has a surface to which the monoclonal antibody that is secreted by the hybridoma cells can bind is dipped into the plate. Each memory is programmed with information that describes the cell line that is contained in the well of the plate into which each matrix with memory is dipped. The matrices with memories are then incubated with antigen and the desired matrices with memories are selected. The selected matrices with memories contain the information as to the identification of the hybridoma secreting the desired monoclonal antibody.

Although this section describes dipping matrices with memories into microtiter plates, it should be apparent that it does not teach that the matrices with memories are present as projections on a second substrate, wherein the projection s each comprise an array location comprising a plurality of discrete sites, wherein the sites comprise different bioactive agents. Rather, it is clear from this disclosure that whatever the material that is dipped comprises an activated surface containing no bioactive agents. After dipping, only one type of bioactive agent becomes attached to the surface. Additionally, the wells of the microtiter plate, into which the matrices with memories are dipped, do not comprise a plurality of different target analytes as required by claim 29. Rather, only a single type of antibody is present in each well. Accordingly, Nova et al. does not disclose at least these three elements of independent claim 29.

The final occurrence of dipping, which appears at column 140, lines 23-36, states the following:

> The glucose oxidase/catalase membrane 5820 is added into the cavity 5818 in the silicone rubber sheath 5816 over the top electrodes using a glutaraldehyde crosslinking solution. After the membrane 5820 is crosslinked, the complete implant is rinsed in sterile solution. The matrix material 5822 is then added by spray or dip coating the entire outer surface of the implant except for the axial end of cavity 5818 where the glucose oxidase membrane 5820 contacts the solution. After completion, the unit is sterilized using gamma or e-beam radiation or ETO. From this point, the implant must be handled under sterile conditions. A pre-implant calibration is performed and this information is downloaded into the implant memory, making the implant ready for implantation.

Column 140, lines 23-36.

As with the first five sections that discuss dipping, here the Nova et al. reference again discloses coating a memory with a matrix. In particular, this example describes coating an implant with a matrix material by either spray coating or dip coating. This disclosure of dipping does not teach that the matrices with memories are present as projections of a second substrate, wherein the projections each comprise an array location comprising a plurality of discrete sites, wherein the sites comprise different bioactive agents or that the material into which the memory is dipped comprises a plurality of different target analytes. Rather, this disclosure simply describes coating an implantable memory with a matrix.

To summarize, most of the dipping described by Nova et al. concerns dipping a memory into a matrix coating so as to associate the memory with the matrix. In the one occurrence where dipping a matrix with a memory into a well is discussed, Nova et al. do not disclose (1) that the matrix with the memory is present as projections of a second substrate (2) comprising an array location comprising a plurality of discrete sites, wherein the site comprise different bioactive

agents. Furthermore, it is not disclosed (3) that the wells into which the matrices with memories are dipped comprise a plurality of target analytes. As such, the Nova et al. reference is devoid of any disclosure that teaches all of the elements of the method recited in independent claim 29 or any of the methods recited in the above-rejected claims dependent on claim 29.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 29, 30, 33, 34, 38-45 and 48-52 as anticipated by Nova et al.

Rejection of claims 31, 32, 35-37 and 45-47 under 35 U.S.C. § 103(a)

The Examiner rejects claims 31, 32, 35-37 and 45-47 under 35 U.S.C. § 103(a) as allegedly obvious over Nova et al. in view of U.S. Patent No. 6,340,588 (Fodor et al.). Although the Examiner acknowledges that Nova et al. do not disclose the elements claims 31, 32, 35-37 and 45-47, the Examiner asserts that Fodor et al. provide these missing elements. The Examiner further alleges that a skilled artisan would be motivated to combine the disclosure of Nova et al. with that of Fodor et al. to arrive at the methods recited in the above-rejected claims with a reasonable expectation of success.

Applicants submit that claims 31, 32, 35-37 and 45-47 are not obvious over Nova et al. in view of Fodor et al. As discussed above, Nova et al. do not disclose the step of dipping the projections of the second substrate into said assay wells as recited in independent claim 29. Fodor et al. do not remedy this deficiency. Accordingly, the combination of Nova et al. and Fodor et al. do not disclose all of the elements of independent claim 29 nor does this combination disclose the all of the elements of the above-rejected claims, which depend from claim 29.

In view of the foregoing remarks, Applicant requests that the Examiner withdraw the rejection of claims 31, 32, 35-37 and 45-47 as obvious in view of the combination of Nova et al. and Fodor et al.

Rejection of claim 55 under 35 U.S.C. § 103(a)

The Examiner rejects claim 55 under 35 U.S.C. § 103(a) as allegedly obvious over Nova et al. in view of U.S. Patent No. 6,269,846 (Overbeck et al.). Although the Examiner acknowledges that Nova et al. do not disclose that the projections are used to stir the sample solutions in the assay wells as recited in claim 55, the Examiner asserts that Overbeck et al.

provide this missing element. The Examiner further alleges that a skilled artisan would be motivated to combine the disclosure of Nova et al. with that of Overbeck et al. to arrive at the methods recited in the above-rejected claims with a reasonable expectation of success.

Applicants submit that claim 55 is not obvious over Nova et al. in view of Overbeck et al. As discussed above, Nova et al. do not disclose the step of dipping the projections of the second substrate into said assay wells as recited in independent claim 29. Overbeck et al. do not remedy this deficiency. Accordingly, the combination of Nova et al. and Overbeck et al. do not disclose all of the elements of independent claim 29 nor does this combination disclose the all of the elements claim 55, which depends from claim 29.

In view of the foregoing remarks, Applicant requests that the Examiner withdraw the rejection of claim 55 as obvious in view of the combination of Nova et al. and Overbeck et al.

Rejection of claims 29-51 under the doctrine of obviousness-type double patenting

The Examiner rejects claims 29-51 under the doctrine of obviousness-type double patenting as allegedly unpatentable over claims 6-24 and 31-58 of U.S. Patent No. 7,060,431 (the '431 patent). In particular, the Examiner asserts that claims 29-51 are not patentably distinct from claims 6-24 and 31-58 of the '431 patent because claims 6-24 and 31-58 allegedly recite the genus of "contacting" and currently pending claims 29-51 recite a species of dipping. Applicants cannot agree.

Claims 29-51 of the instant application recite methods of determining the presence or absence of a plurality of analytes. These methods recite, in relevant part, the steps of (a) providing a first substrate with a surface comprising a plurality of assay wells; (b) providing a second substrate; (c) dipping the projections of the second substrate into said assay wells; and (d) detecting the presence or absence of said target analytes. The Examiner asserts that since claims 6-24 and claims 31-58 of the '431 patent recite, in relevant part, the step of (a) contacting a sample with an array, they disclose a genus of methods for contacting a sample with a substrate. The Examiner then alleges that dipping projections of a second substrate into assay wells of a first substrate constitutes a species of this genus, which is alleged to be obvious. Applicants do agree that dipping is but one of the myriad species included in the incredibly vast genus of contacting. However, Applicants would like to remind the Examiner that the Examiner has the

burden of establishing a prima facie case of why a species would by obvious in view of a disclosed genus. See MPEP § 2144.08. The Examiner has not met this burden.

In view of the foregoing remarks, Applicants respectfully submit that claims 29-51 are not obvious in view of claim 6-24 and 31-58 of the '431 patent. As such, Applicants respectfully request that the Examiner withdraw the rejection of claims 29-51 under the doctrine of obviousness-type double patenting.

Rejection of claims 29-51 under the doctrine of obviousness-type double patenting

The Examiner rejects claims 29-51 under the doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-5 and 9 of U.S. Patent No. 6,858,394 (the '394 patent). In particular, the Examiner asserts that claims 29-51 are not patentably distinct from claims 1-5 and 9 of the '394 patent because claims 1-5 and 9 allegedly recite the genus of "contacting" and currently pending claims 29-51 recite a species of dipping. Again, Applicants cannot agree.

Although the substance of this rejection was not discussed during the interview of September 4, 2008, Applicants note that the Examiner's rejection of claims 29-51 in view of the '394 patent is based on the same assertion made in connection with the '431 patent. As discussed above, Applicants respectfully submit that, even if dipping is a species of the term "contacting," the Examiner has not met the required burden of establishing a prima facie case of why a species would by obvious in view of a disclosed genus. See MPEP § 2144.08.

In view of the foregoing remarks, Applicants respectfully submit that claims 29-51 are not obvious in view of claim 1-5 and 9 of the '349 patent. As such, Applicants respectfully request that the Examiner withdraw the rejection of claims 29-51 under the doctrine of obviousness-type double patenting.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this

application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Co-Pending Applications of Assignee

Applicants wish to remind the Examiner that co-owned U.S. Patent Application No. 10/767,476 is currently pending. The most recent communication in that case was issued August 21, 2008.

## CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: September 16, 2008

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